Unit 3
Cell Metabolism

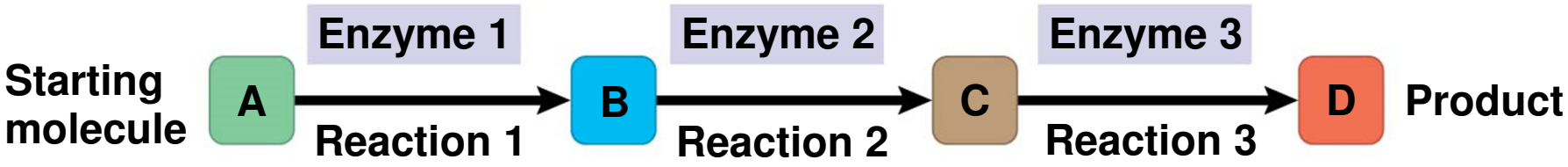
Chapter 6: An Introduction to Metabolism

Overview: The Energy of Life

- The living cell is a miniature chemical factory where thousands of reactions occur
- The cell extracts energy and applies energy to perform work
- Some organisms even convert energy to light, as in bioluminescence

Concept 6.1: An organism's metabolism transforms matter and energy

- **Metabolism** is the totality of an organism's chemical reactions
- Metabolism is an *emergent* property of life that arises from interactions between molecules within the cell
- A **metabolic pathway** begins with a specific molecule and ends with a product
- Each step is catalyzed by a specific enzyme



- **Catabolic pathways =**
  - Release energy by breaking down complex molecules into simpler compounds
    - Example of catabolism: Cellular respiration
  - Breakdown of glucose in the presence of oxygen
- **Anabolic pathways =**
  - Consume energy to build complex molecules from simpler ones
  - Example of anabolism: The synthesis of protein from amino acids

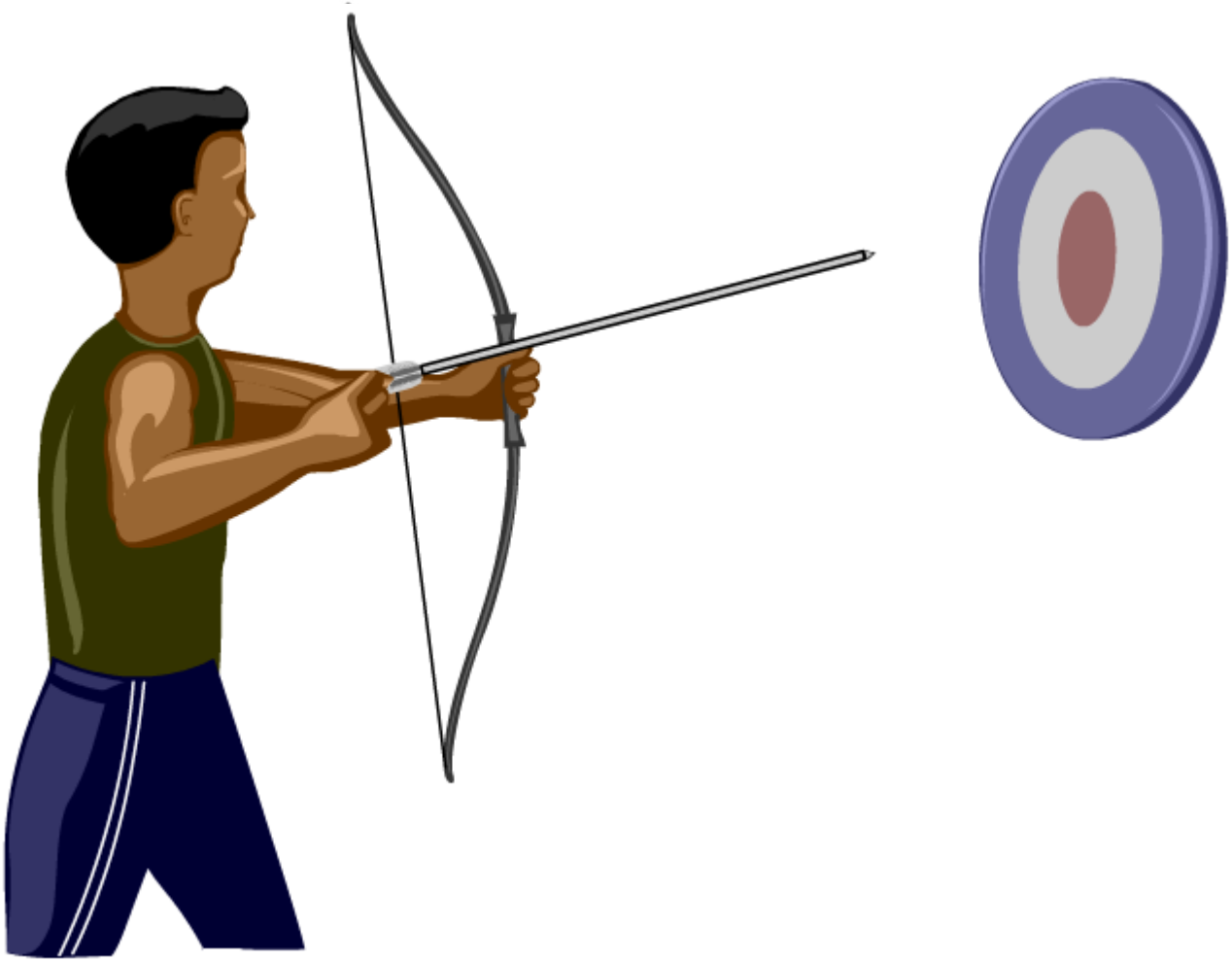
Forms of Energy

- **Energy** is the capacity to cause change
  - Energy exists in various forms, some of which can perform work
- **Kinetic energy** is energy associated with motion
- **Thermal energy** is kinetic energy associated with random movement of atoms or molecules
- **Heat** is thermal energy in transfer from one object to another
- Light is also a type of energy that can harnessed to perform work
  - Photosynthesis

- **Potential energy** is energy that matter possesses because of its location or structure
- **Chemical energy** is potential energy available for release in a chemical reaction

- Energy can be converted from one form to another
  - Energy flows into most ecosystems in the form of light and exits in the form of heat

- **Bioenergetics** is the study of how energy flows through living organisms



Animation: Energy Concepts
Right click slide / Select play

Figure 6.2

A diver has more potential energy on the platform.
Diving converts potential energy to kinetic energy.
Climbing up converts the kinetic energy of muscle movement to potential energy.
A diver has less potential energy in the water.

The Laws of Energy Transformation

- **Thermodynamics** is the study of energy transformations
- An isolated system, such as that approximated by liquid in a thermos, is isolated from its surroundings
- In an open system, energy and matter can be transferred between the system and its surroundings
  - Organisms are open systems

The First Law of Thermodynamics

- According to the **first law of thermodynamics**, the energy of the universe is constant
  - *Energy can be transferred and transformed, but it cannot be created or destroyed*
- The first law is also called the *principle of conservation of energy*

- Note: Some energy is converted to thermal energy and released as heat
  - Thus unavailable to do work, but NOT destroyed

The Second Law of Thermodynamics

- During every energy transfer or transformation, some energy is unusable and is often lost as heat
- According to the **second law of thermodynamics**
  - *Every energy transfer or transformation increases the entropy of the universe*
- **Entropy** is a measure of disorder, or randomness

- Living cells unavoidably convert organized forms of energy to heat
- **Spontaneous processes** occur without energy input
  - Can happen quickly or slowly
  - “Energetically favorable”
- For a process to occur without energy input, it must increase the entropy of the universe!

Concept 6.2: The free-energy change of a reaction tells us whether or not the reaction occurs spontaneously

- Biologists want to know which reactions occur spontaneously and which require input of energy
- To do so, they need to determine energy changes that occur in chemical reactions

- Gibbs defined a function to describe the tendency of a system to change spontaneously (without considering its surroundings)

Free-Energy Change (ΔG), Stability, and Equilibrium

- A living system's **free energy** is energy that can do work when temperature and pressure are uniform, as in a living cell
- The change in free energy (ΔG) during a chemical reaction is the difference between the free energy of the final state and the free energy of the initial state

$$\Delta G = \Delta H - T\Delta S \qquad \Delta G = G_{\text{final state}} - G_{\text{initial state}}$$

- ΔH = change in the system's enthalpy (heat)
- ΔS = change in the system's entropy (disorder)
- T = absolute temperature in K (K = ℃ + 273)

- ΔG can be used to predict if a process is energetically favorable
  - Only processes with a negative ΔG are spontaneous!
    - IE-No input of energy needed
    - Spontaneous processes can be harnessed to perform work

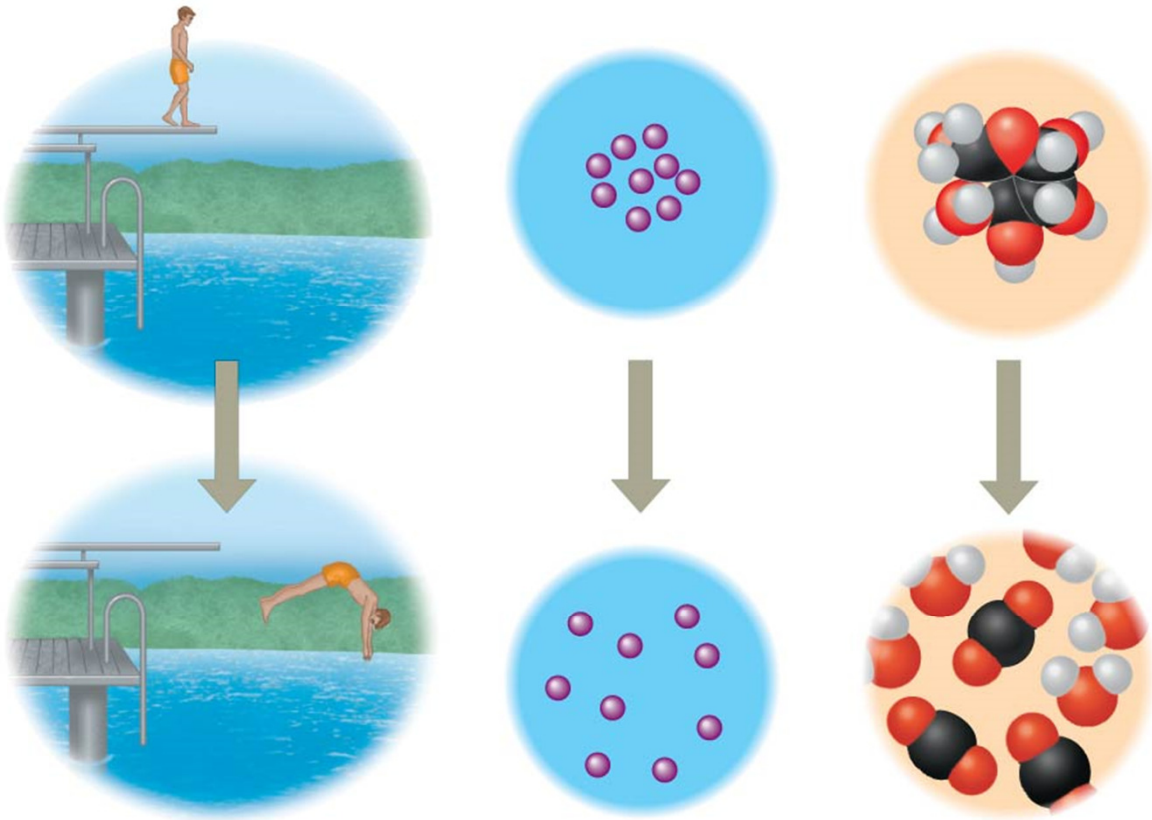
- Free energy is a measure of a system's instability, its tendency to change to a more stable state
- During a spontaneous change, free energy decreases and the stability of a system increases
- At equilibrium, forward and reverse reactions occur at the same rate; it is a state of maximum stability
- A process is spontaneous and can perform work only when it is moving toward equilibrium

Figure 6.5

- More free energy (higher *G*)
- Less stable
- Greater work capacity

In a spontaneous change
- The free energy of the system decreases ($\Delta G < 0$)
- The system becomes more stable
- The released free energy can be harnessed to do work

- Less free energy (lower *G*)
- More stable
- Less work capacity



(a) Gravitational motion

(b) Diffusion

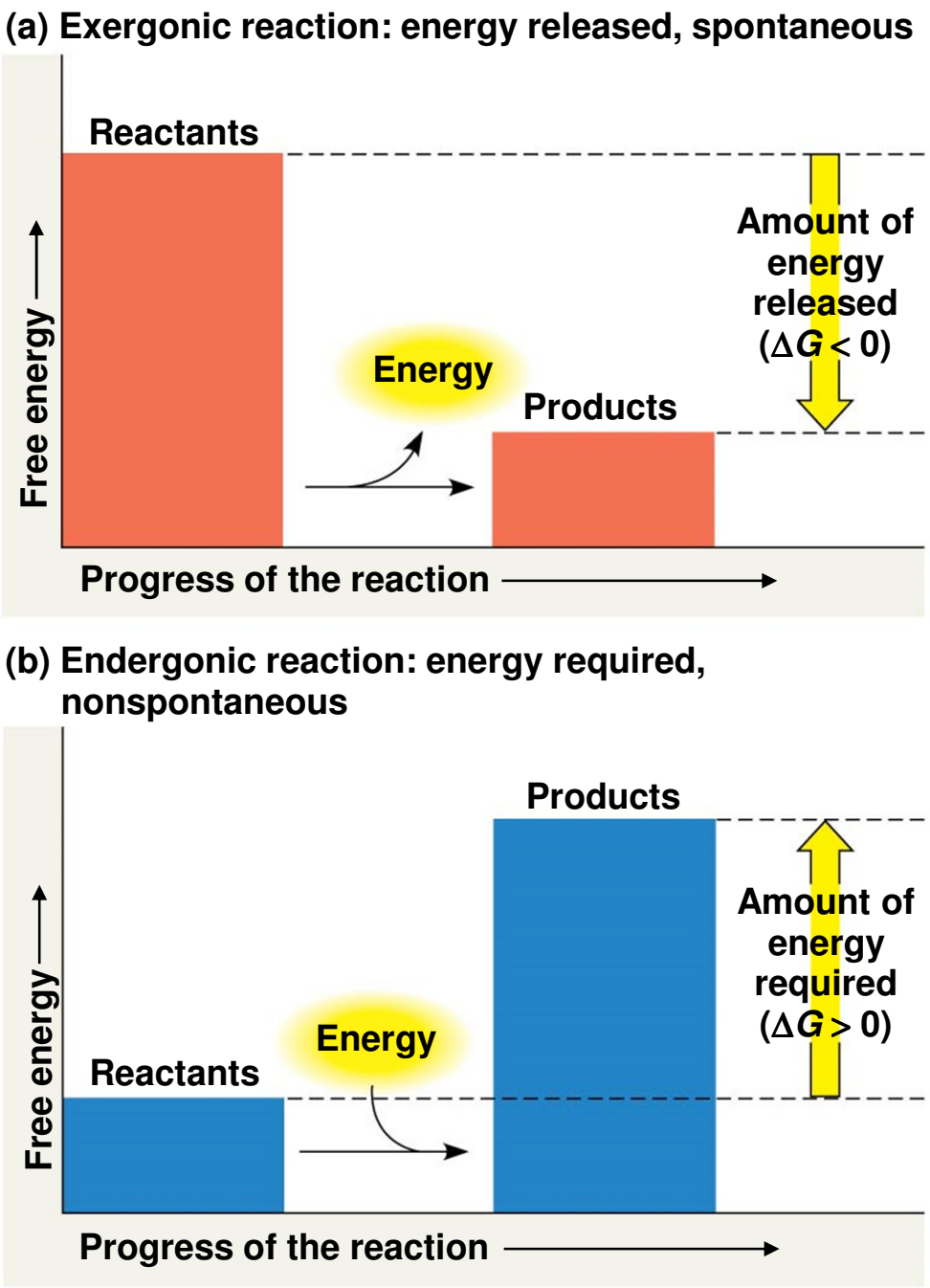
(c) Chemical reaction

Exergonic and Endergonic Reactions in Metabolism

- An **exergonic reaction** proceeds with a net release of free energy
  - ΔG is negative
  - Spontaneous (energetically favorable)
- The magnitude of ΔG represents the maximum amount of work the reaction can perform

- An **endergonic reaction** absorbs free energy from its surroundings
  - ΔG is positive
  - Nonspontaneous
- The magnitude of ΔG is the quantity of energy required to drive the reaction

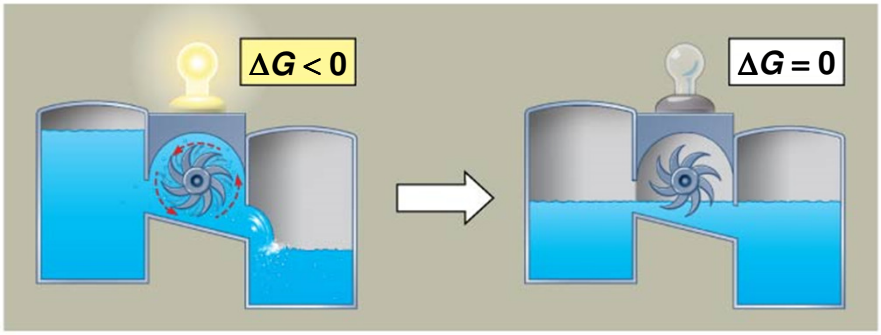
Figure 6.6


(a) Exergonic reaction: energy released, spontaneous
Reactants
Energy
Products
Amount of energy released ($\Delta G < 0$)
Free energy
Progress of the reaction
(b) Endergonic reaction: energy required, nonspontaneous
Products
Energy
Reactants
Amount of energy required ($\Delta G > 0$)
Free energy
Progress of the reaction

Equilibrium and Metabolism

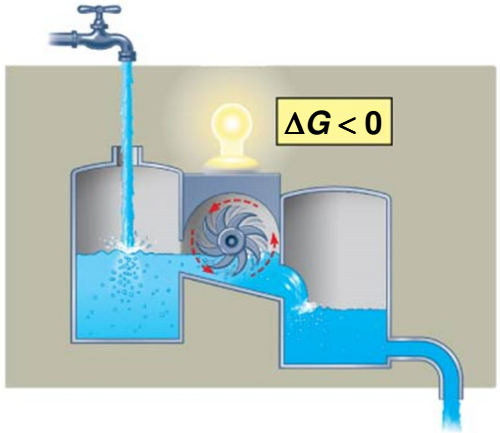
- Reactions in a closed system eventually reach equilibrium and then do no work
- Cells are not in equilibrium; they are OPEN systems experiencing a constant flow of materials
  - A defining feature of life is that metabolism is never at equilibrium!

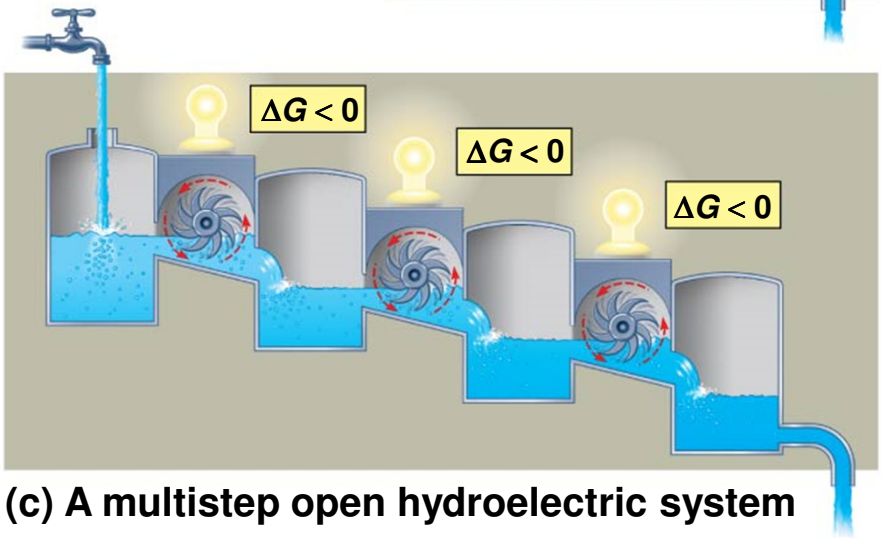
Figure 6.7



(a) An isolated hydroelectric system

(b) An open hydroelectric system





(c) A multistep open hydroelectric system

Concept 6.3: ATP powers cellular work by coupling exergonic reactions to endergonic reactions

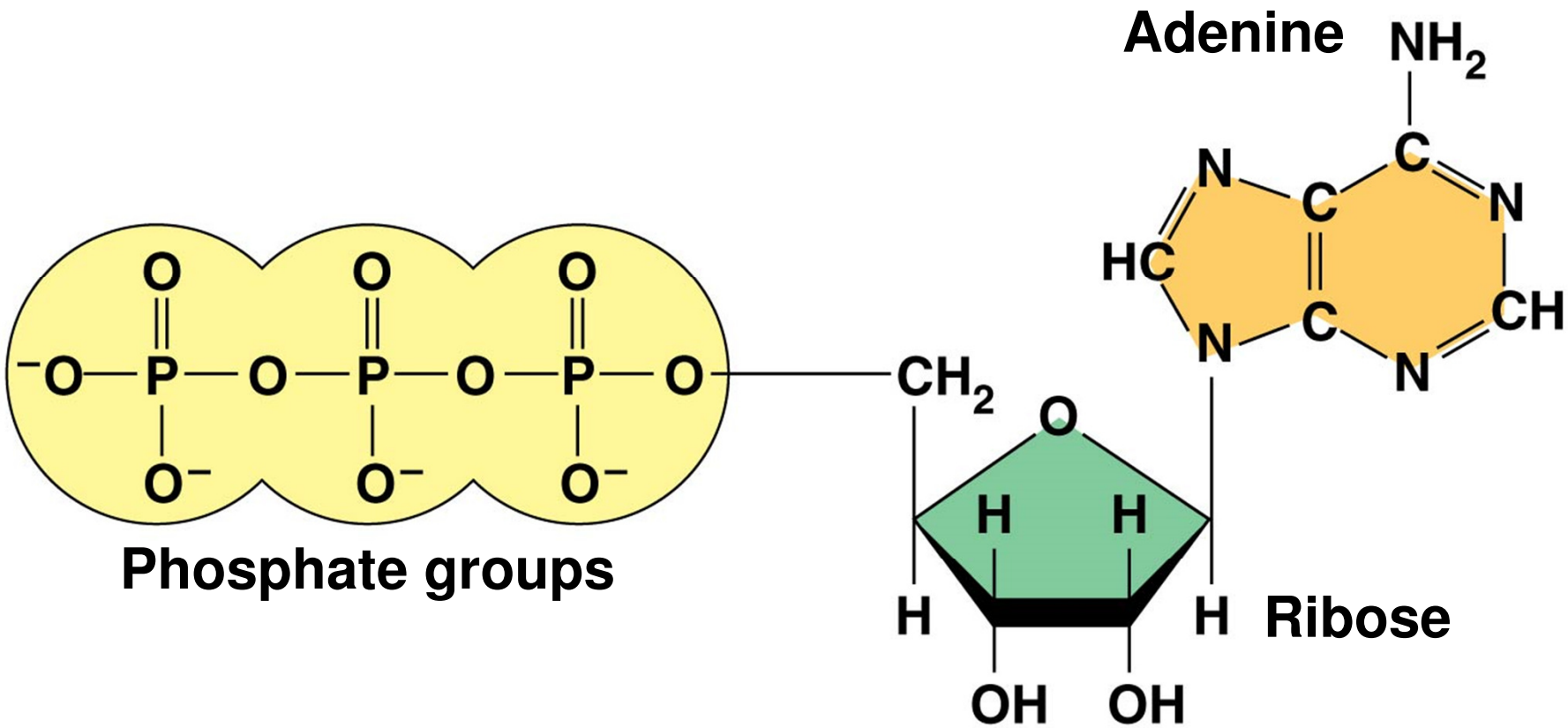
- A cell does three main kinds of work
  - Chemical
    - Ex: Synthesis of polymers from monomers
  - Transport
    - Ex: Pumping of substances across membrane against concentration gradient
  - Mechanical
    - Ex: Contraction of muscle cells

- To do work, cells manage energy resources by **energy coupling**
  - The use of an exergonic process to drive an endergonic one
- Most energy coupling in cells is mediated by ATP

The Structure and Hydrolysis of ATP

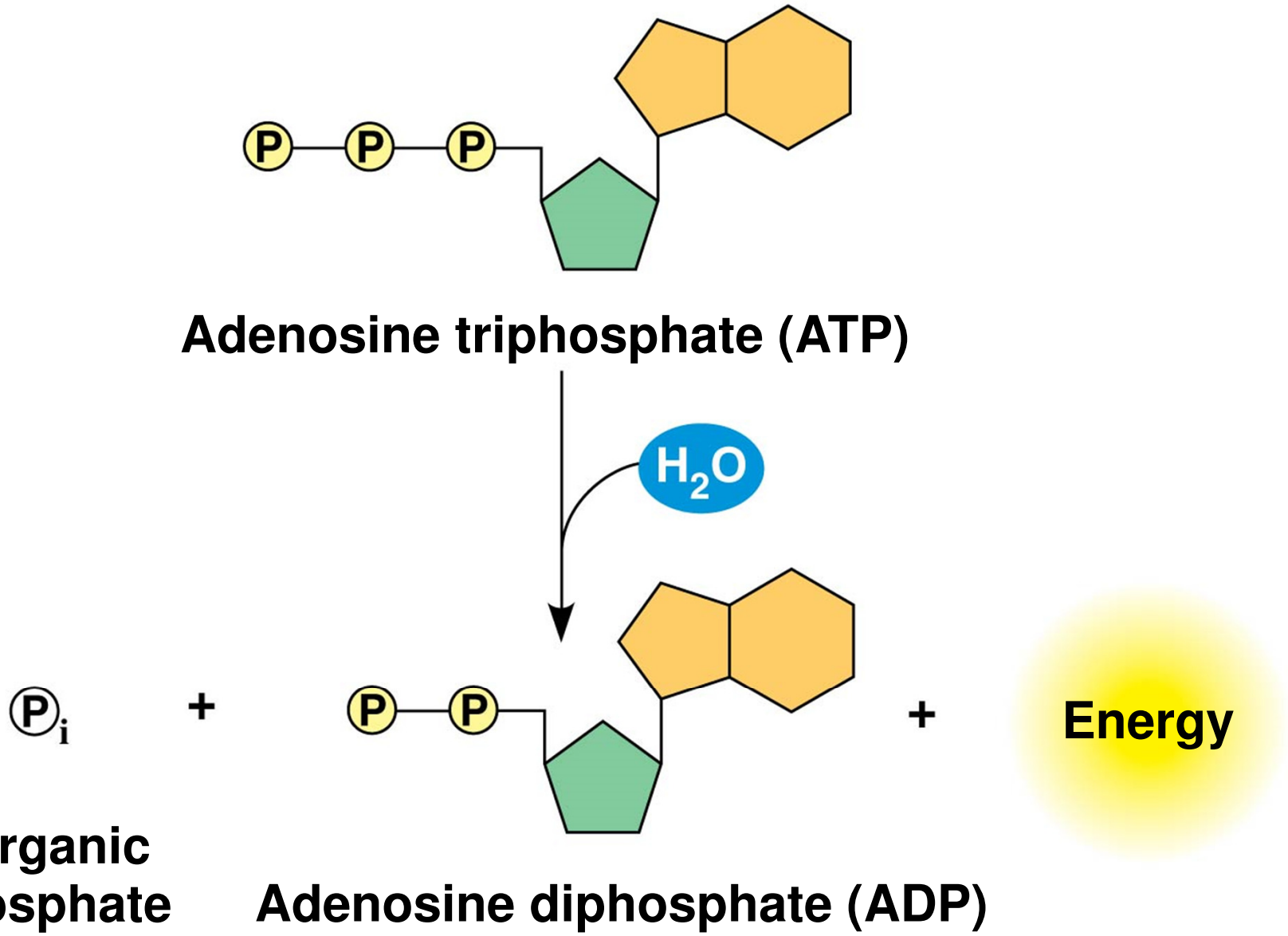
- **ATP (adenosine triphosphate)** is composed of
  - Ribose (a sugar)
  - Adenine (a nitrogenous base)
  - Three phosphate groups
- In addition to its role in energy coupling, ATP is also used to make RNA

Figure 6.8a



(a) The structure of ATP

Figure 6.8b



(b) The hydrolysis of ATP

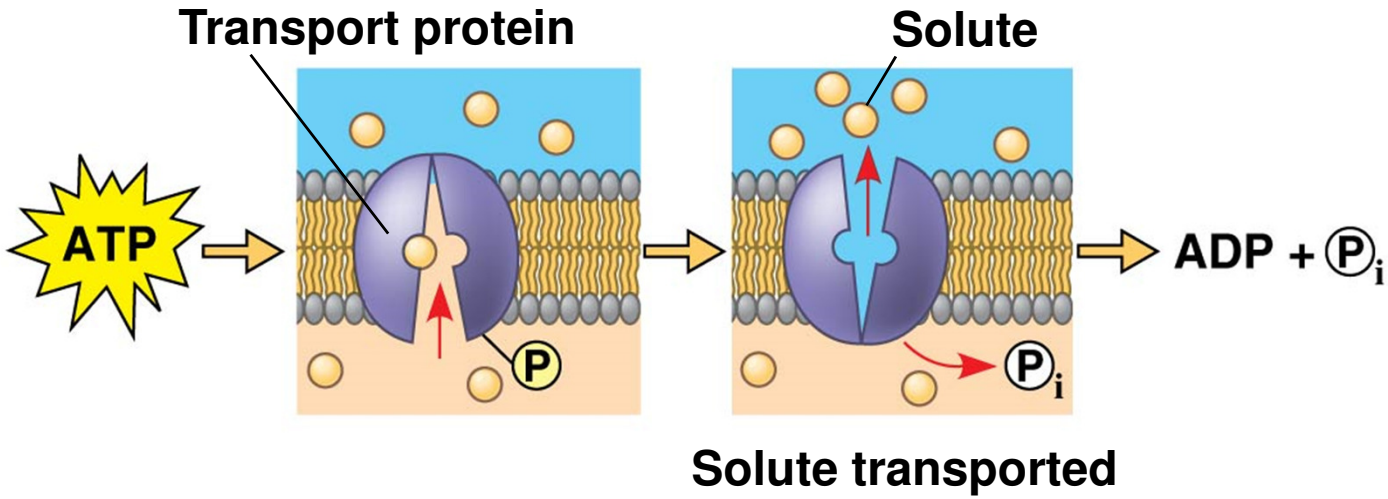
- The bonds between the phosphate groups of ATP can be broken by hydrolysis
- Energy is released from ATP when the terminal phosphate bond is broken
  - This release of energy comes from the chemical change to a state of lower free energy, not from the phosphate bonds themselves
  - Exergonic

How the Hydrolysis of ATP Performs Work

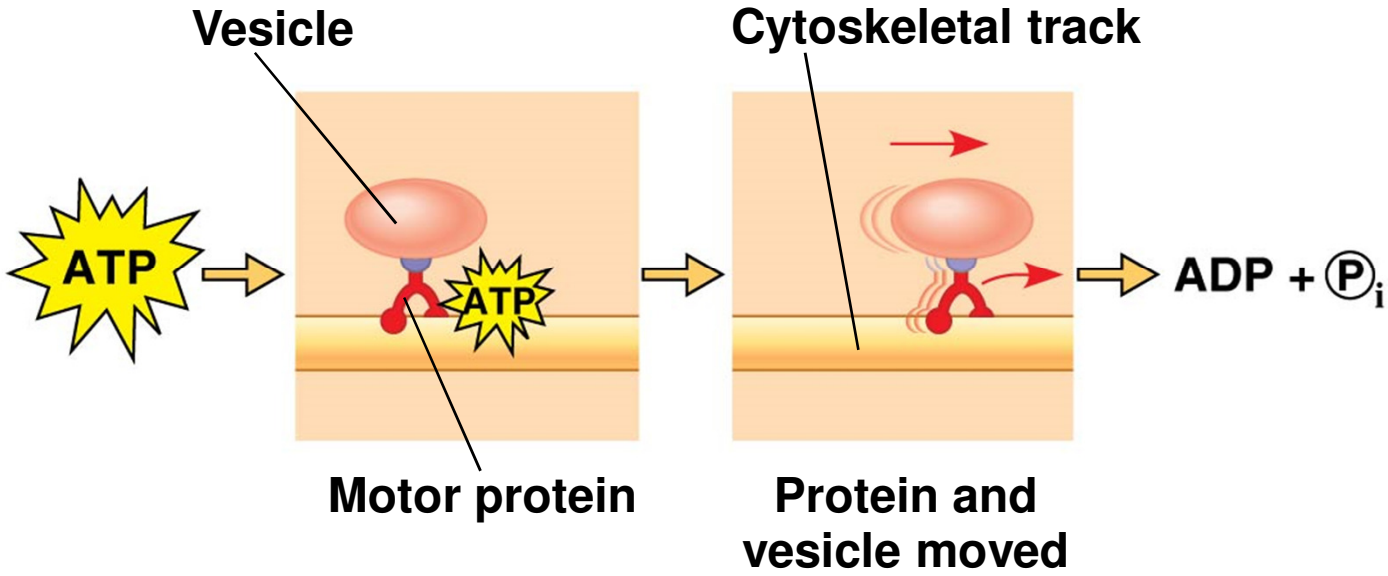
- The three types of cellular work (mechanical, transport, and chemical) are powered by the hydrolysis of ATP
- In the cell, the energy from the exergonic reaction of ATP hydrolysis can be used to drive an endergonic reaction
- *Overall*, the coupled reactions are exergonic

- ATP drives endergonic reactions by *phosphorylation*, transferring a phosphate group to some other molecule, such as a reactant
  - The recipient molecule is now called a **phosphorylated intermediate**
- ATP hydrolysis leads to a change in a protein's <u>shape</u> and often its ability to bind to another molecule

Figure 6.10



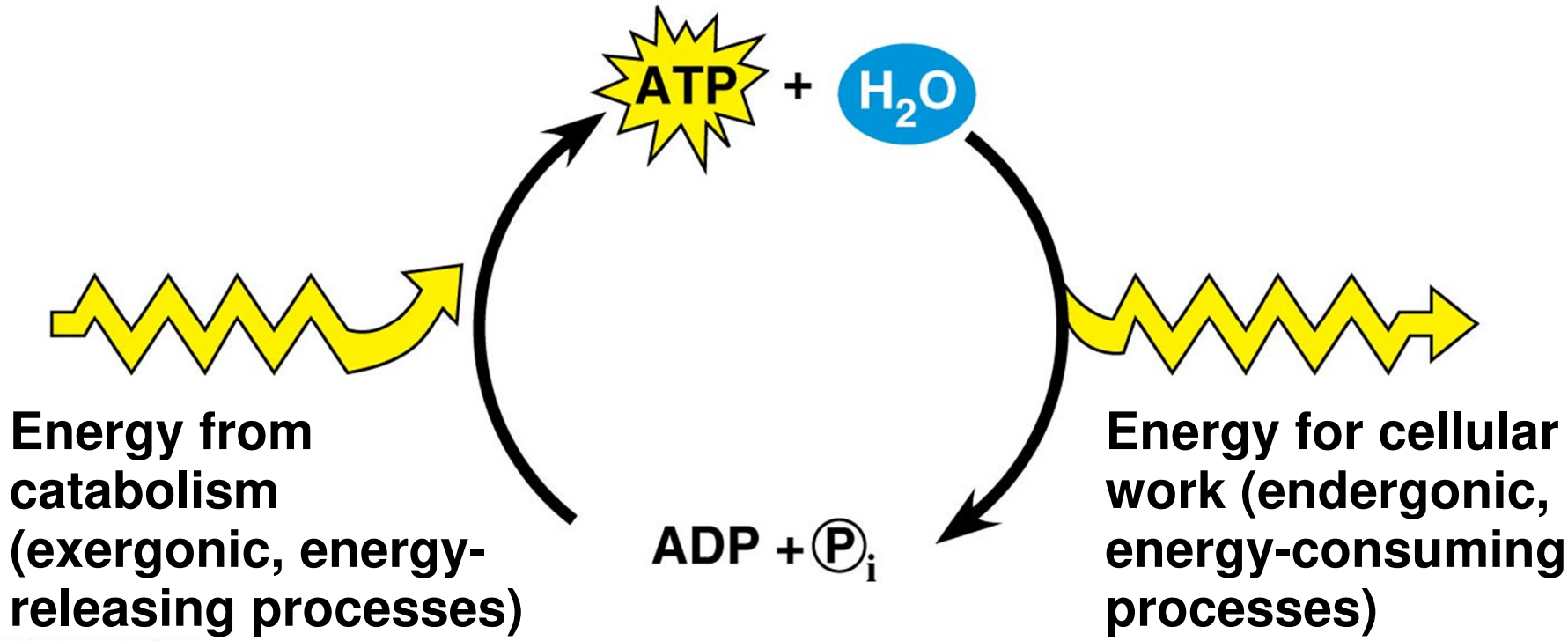
(a) Transport work: ATP phosphorylates transport proteins.



(b) Mechanical work: ATP binds noncovalently to motor proteins and then is hydrolyzed.

The Regeneration of ATP

- ATP is a renewable resource that is regenerated by addition of a phosphate group to adenosine diphosphate (ADP)



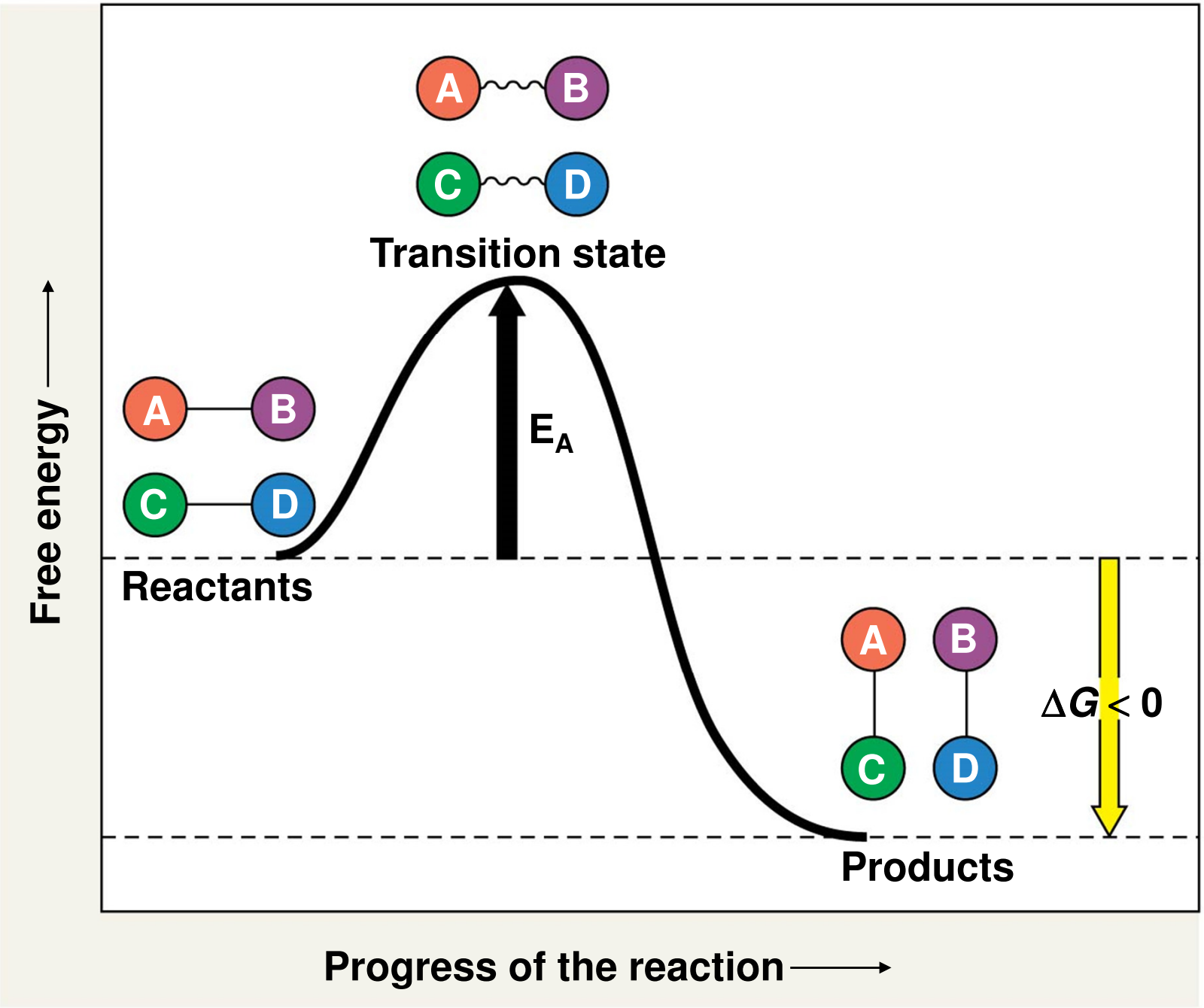
Concept 6.4: Enzymes speed up metabolic reactions by lowering energy barriers

- A **catalyst** is a chemical agent that
  - Speeds up a reaction
  - Without being consumed by the reaction
- An **enzyme** is a catalytic protein

The Activation Energy Barrier

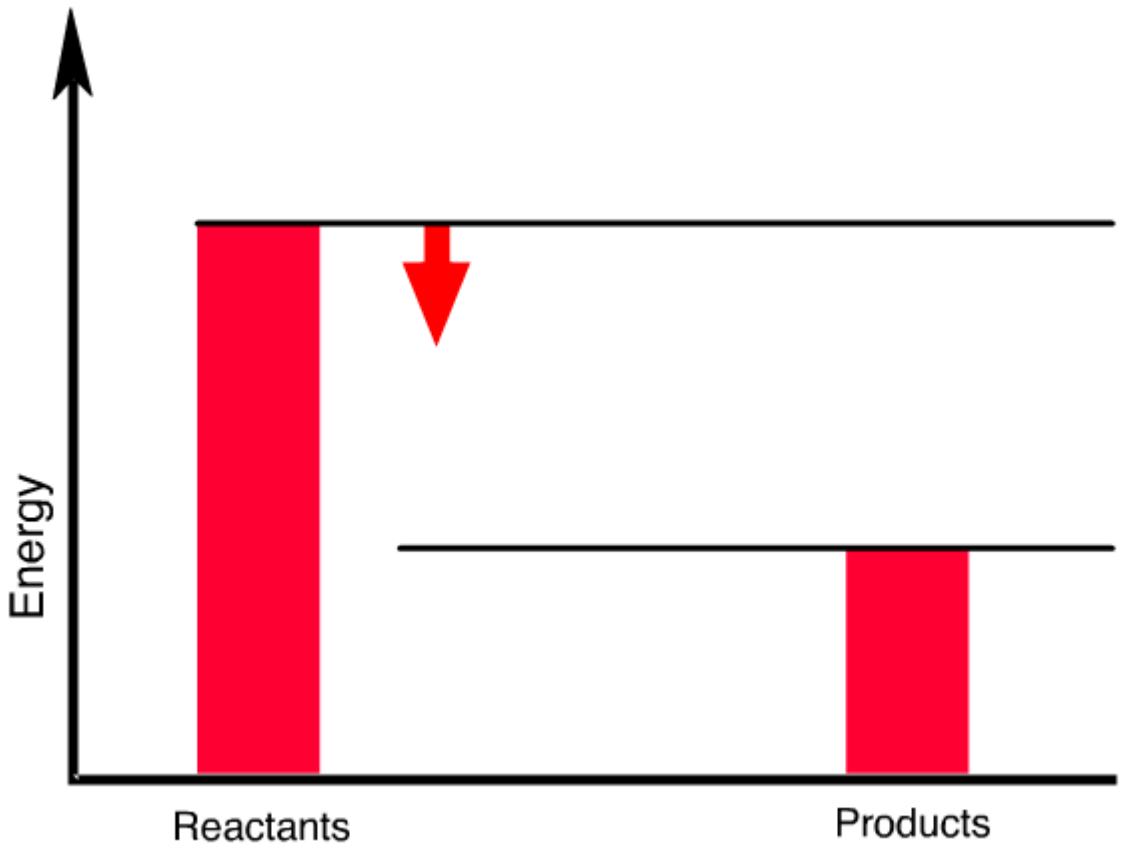
- Every chemical reaction between molecules involves bond breaking and bond forming
- The initial energy needed to start a chemical reaction is called the **activation energy** (E_A)
  - Activation energy is often supplied in the form of thermal energy that the reactant molecules absorb from their surroundings

Figure 6.12


A
B
C
D
Transition state
E_A
Reactants
Products
$\Delta G < 0$
Free energy
Progress of the reaction

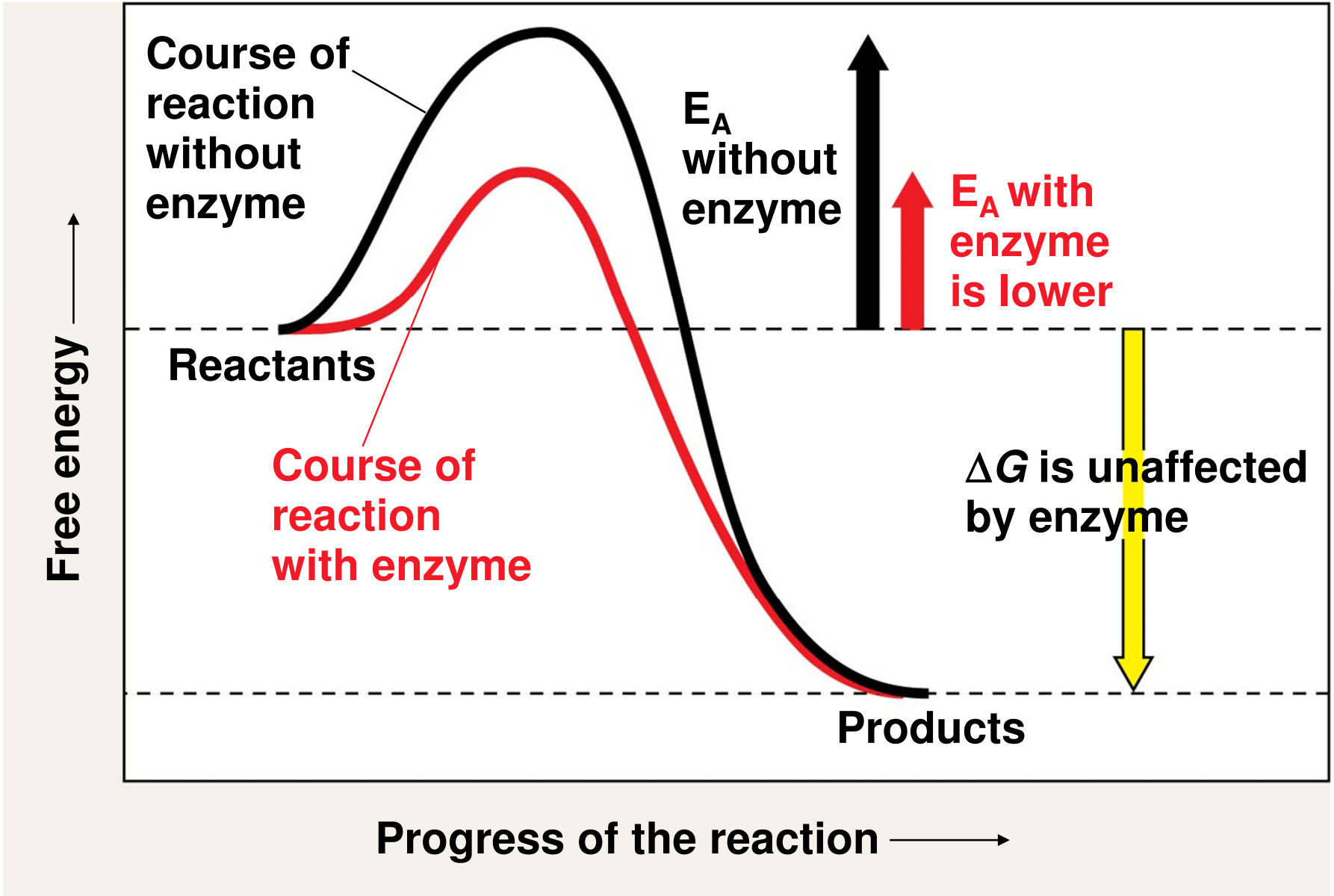
How Enzymes Speed Up Reactions

- Enzymes catalyze reactions by lowering the E_A barrier
- Enzymes do not affect the change in free energy (ΔG)!
  - Cannot make an endergonic reaction exergonic!
  - Instead, they hasten reactions that would occur eventually
- Enzymes are very <u>specific</u> for the reactions they catalyze



Animation: How Enzymes Work
Right click slide / Select play

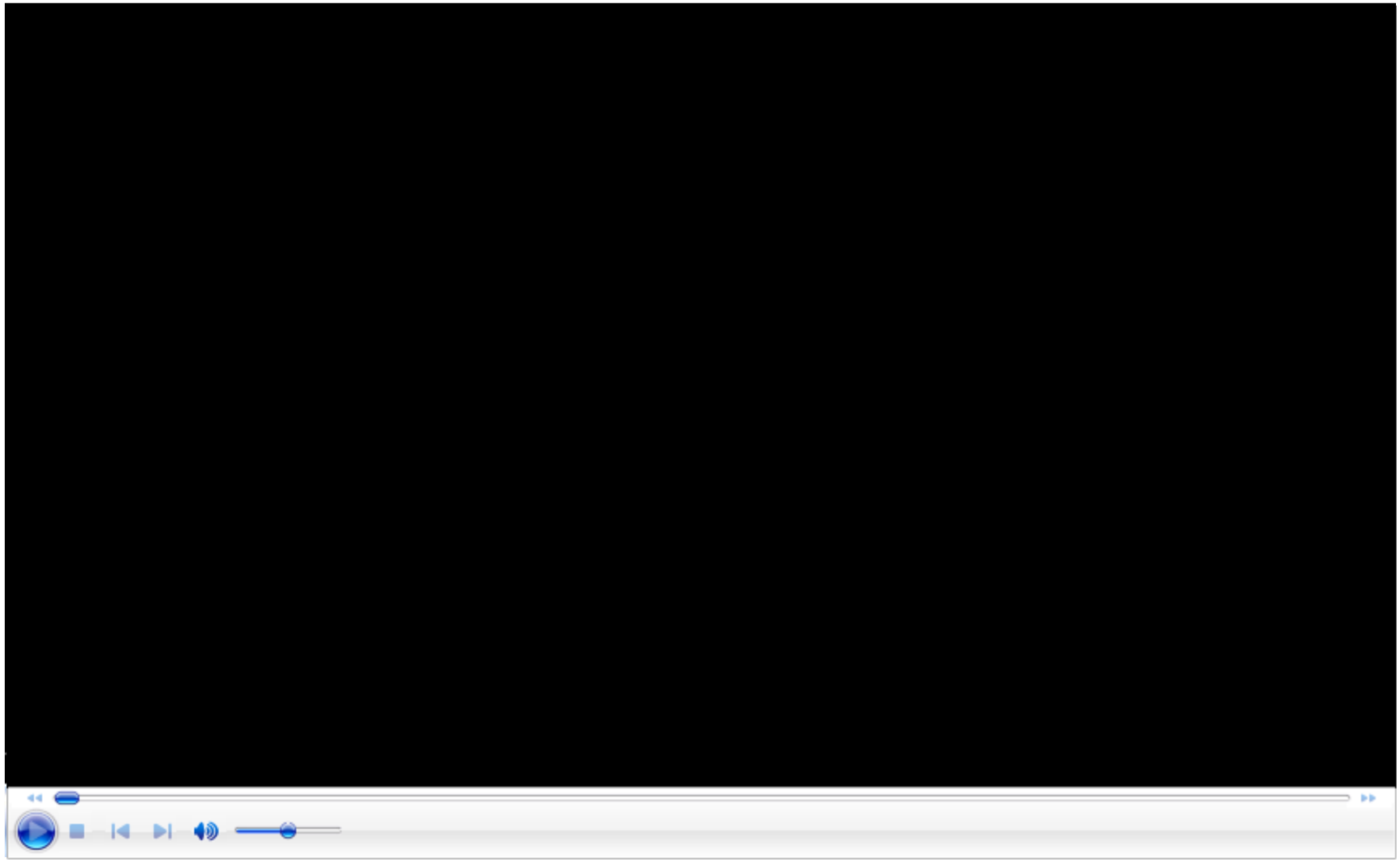
Figure 6.13


Course of reaction without enzyme
E_A without enzyme
E_A with enzyme is lower
Reactants
Course of reaction with enzyme
ΔG is unaffected by enzyme
Products
Free energy
Progress of the reaction

Substrate Specificity of Enzymes

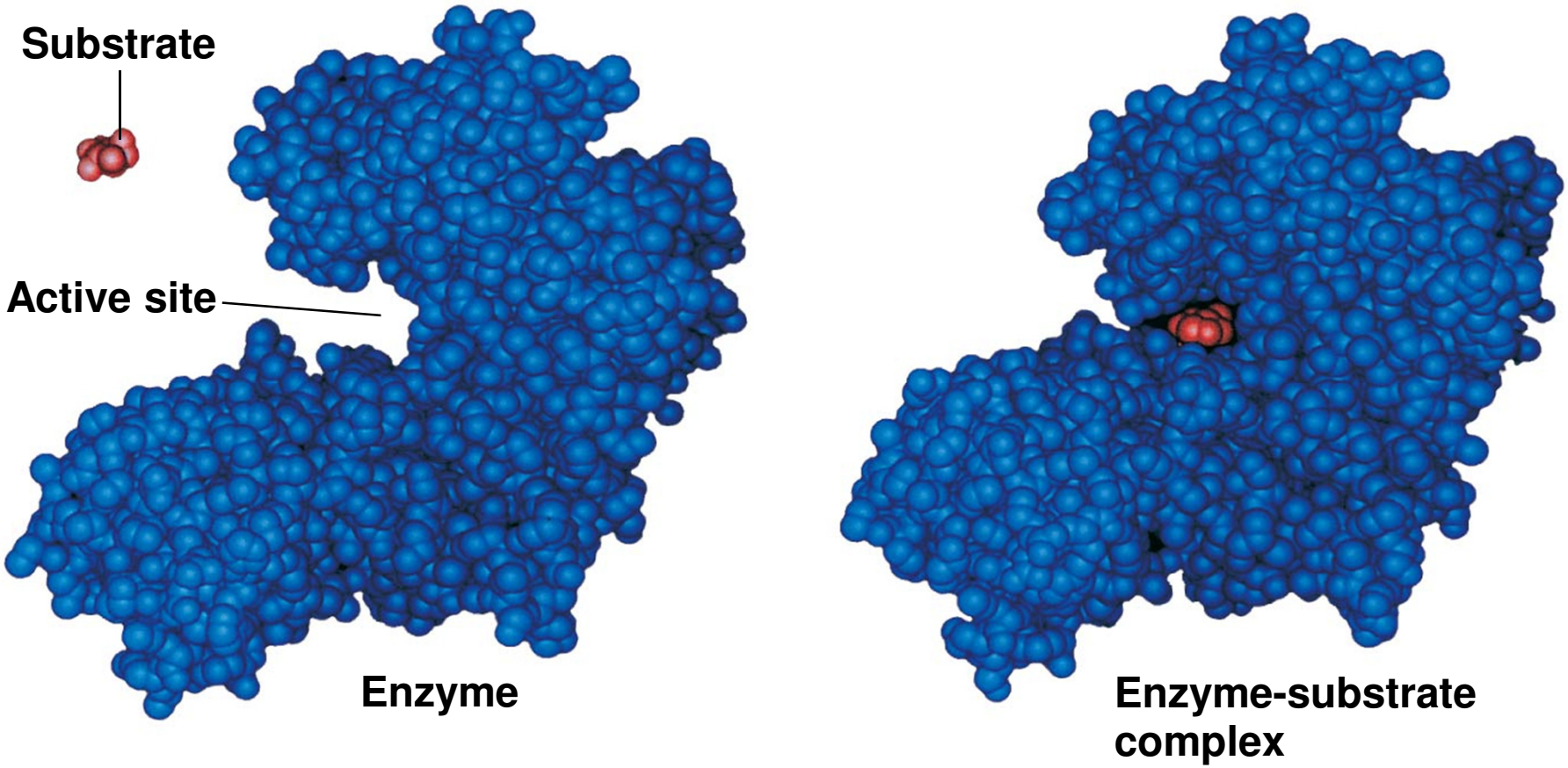
- The reactant that an enzyme acts on is called the enzyme's **substrate**
- The enzyme binds to its substrate, forming an **enzyme-substrate complex**
- The **active site** is the region on the enzyme where the substrate binds
- Enzyme specificity results from the complementary fit between the <u>shape</u> of its active site and the substrate <u>shape</u>

- Enzymes change shape due to chemical interactions with the substrate
- This **induced fit** of the enzyme to the substrate brings chemical groups of the active site into positions that enhance their ability to catalyze the reaction



Video: Enzyme Induced Fit

Figure 6.14



Catalysis in the Enzyme's Active Site

- In an enzymatic reaction, the substrate binds to the active site of the enzyme
- The active site can lower an E_A barrier by
  - Orienting substrates correctly
  - Straining substrate bonds
  - Providing a favorable microenvironment
  - Covalently bonding to the substrate
- Enzymes can be used over and over again because they emerge from the reaction in their original form

Figure 6.15-1

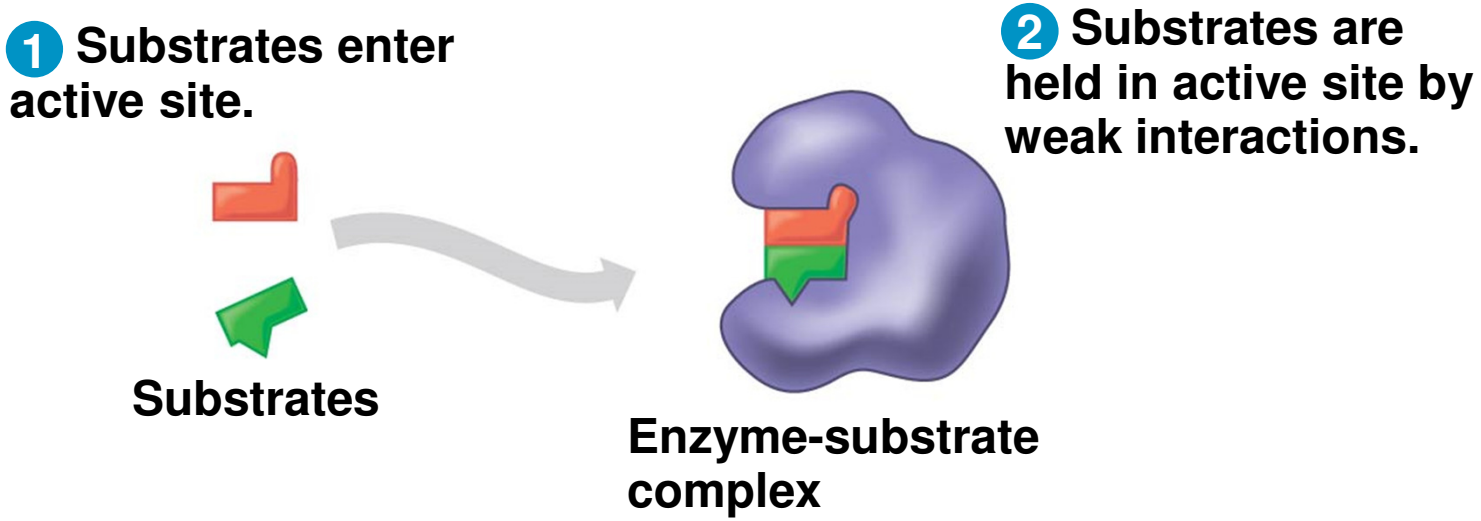

1 Substrates enter active site.
2 Substrates are held in active site by weak interactions.
Substrates
Enzyme-substrate complex

Figure 6.15-2

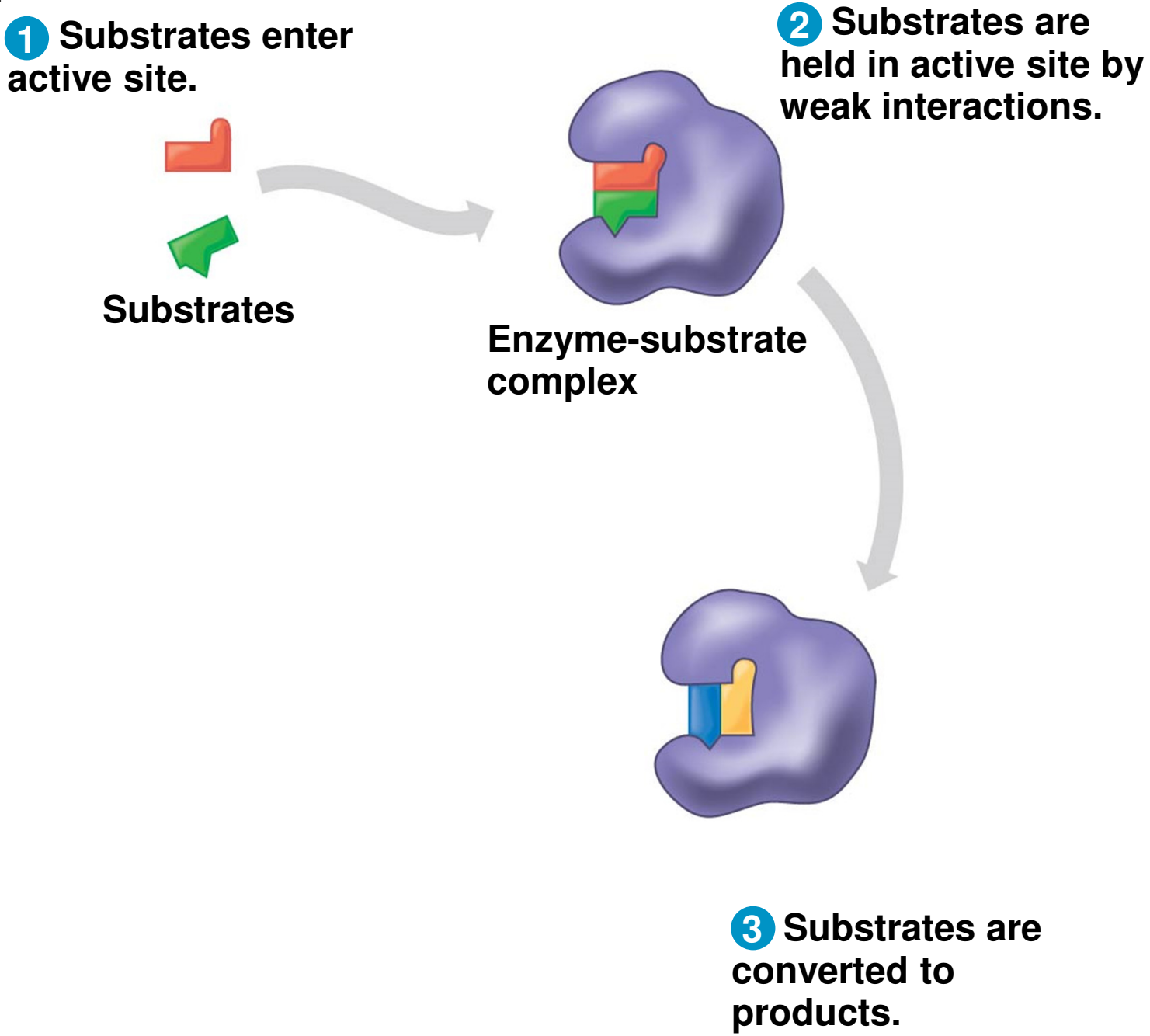

1 Substrates enter active site.
Substrates
2 Substrates are held in active site by weak interactions.
Enzyme-substrate complex
3 Substrates are converted to products.

Figure 6.15-3

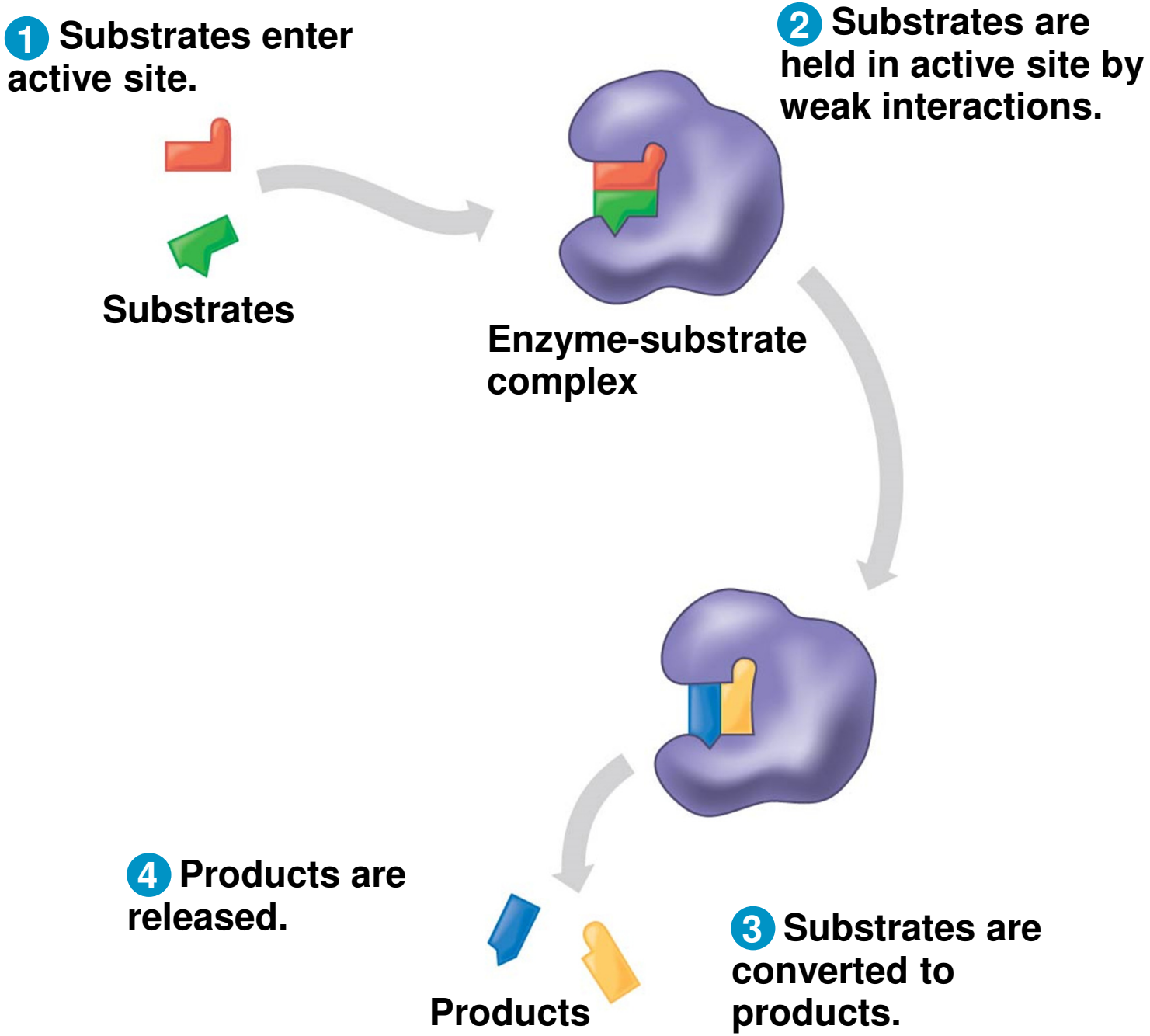
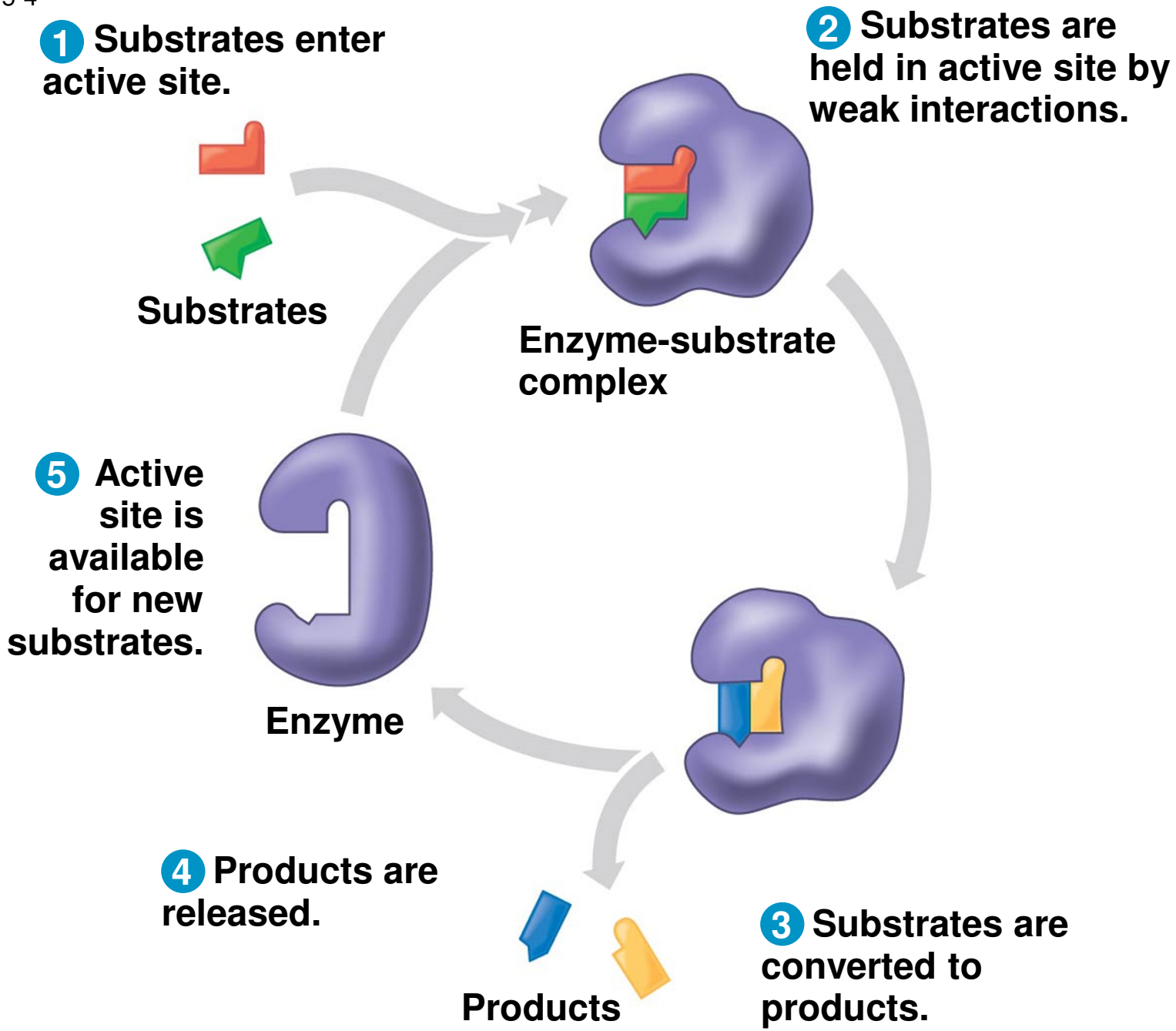

1 Substrates enter active site.
Substrates
2 Substrates are held in active site by weak interactions.
Enzyme-substrate complex
3 Substrates are converted to products.
4 Products are released.
Products

Figure 6.15-4


1 Substrates enter active site.
Substrates
2 Substrates are held in active site by weak interactions.
Enzyme-substrate complex
3 Substrates are converted to products.
Products
4 Products are released.
Enzyme
5 Active site is available for new substrates.

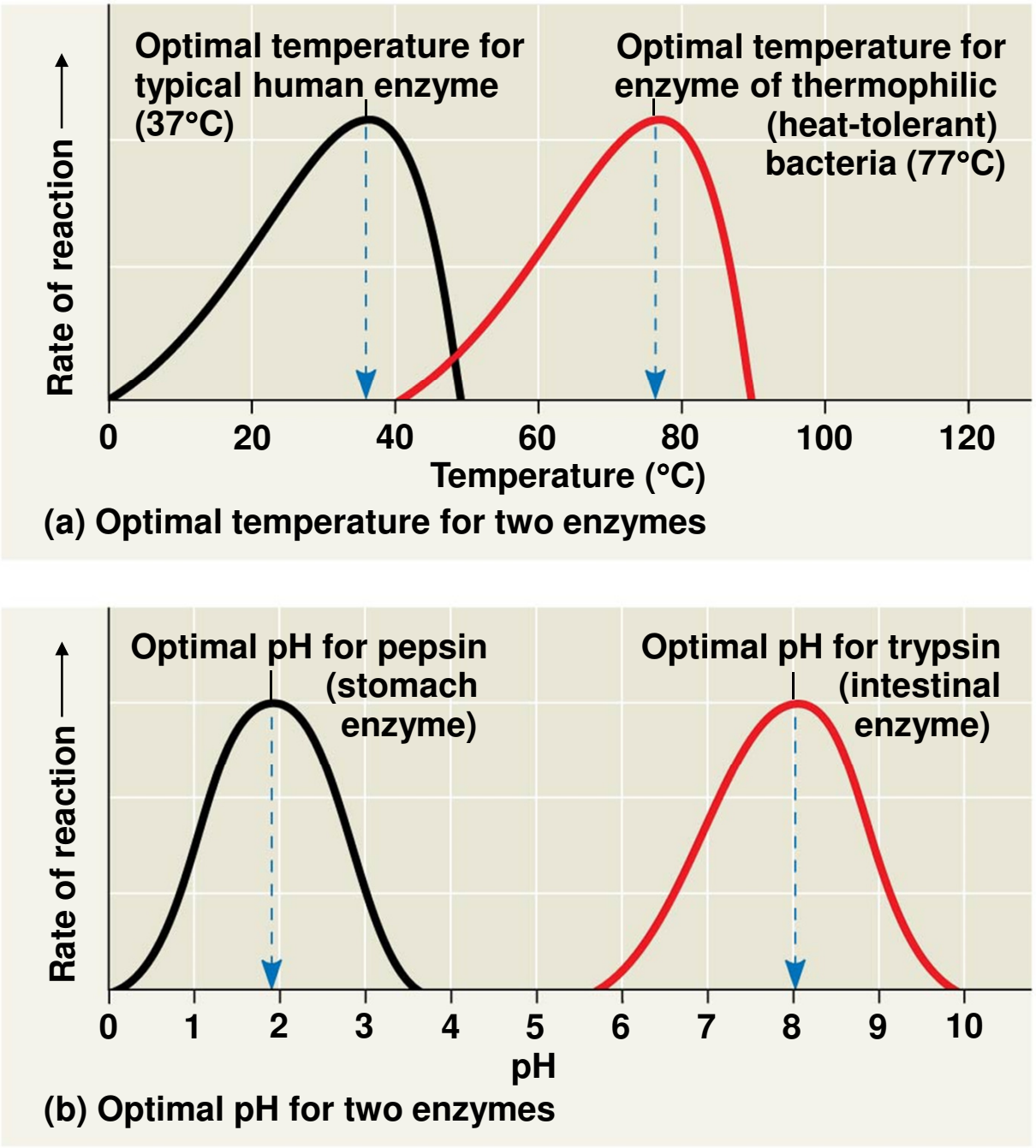
Effects of Local Conditions on Enzyme Activity

- An enzyme's activity can be affected by
  - General environmental factors, such as temperature and pH
  - Chemicals that specifically influence the enzyme

Effects of Temperature and pH

- Each enzyme has an optimal temperature in which it can function
  - Typically, the rate of the reaction increases as the temperature increases, to a point
    - But then speed of reaction drops sharply as the protein *denatures*
- Each enzyme has an optimal pH in which it can function
  - Most fall in range of pH 6-8
- Optimal conditions favor the most active shape for the enzyme molecule

Figure 6.16


Optimal temperature for typical human enzyme (37°C)
Optimal temperature for enzyme of thermophilic (heat-tolerant) bacteria (77°C)
Rate of reaction
0
20
40
60
80
100
120
Temperature (°C)
(a) Optimal temperature for two enzymes
Optimal pH for pepsin (stomach enzyme)
Optimal pH for trypsin (intestinal enzyme)
Rate of reaction
0
1
2
3
4
5
6
7
8
9
10
pH
(b) Optimal pH for two enzymes

Cofactors

- **Cofactors** are nonprotein enzyme helpers
  - Cofactors may be inorganic (such as a metal in ionic form) or organic
- An organic cofactor is called a **coenzyme**
  - Coenzymes include vitamins

Enzyme Inhibitors

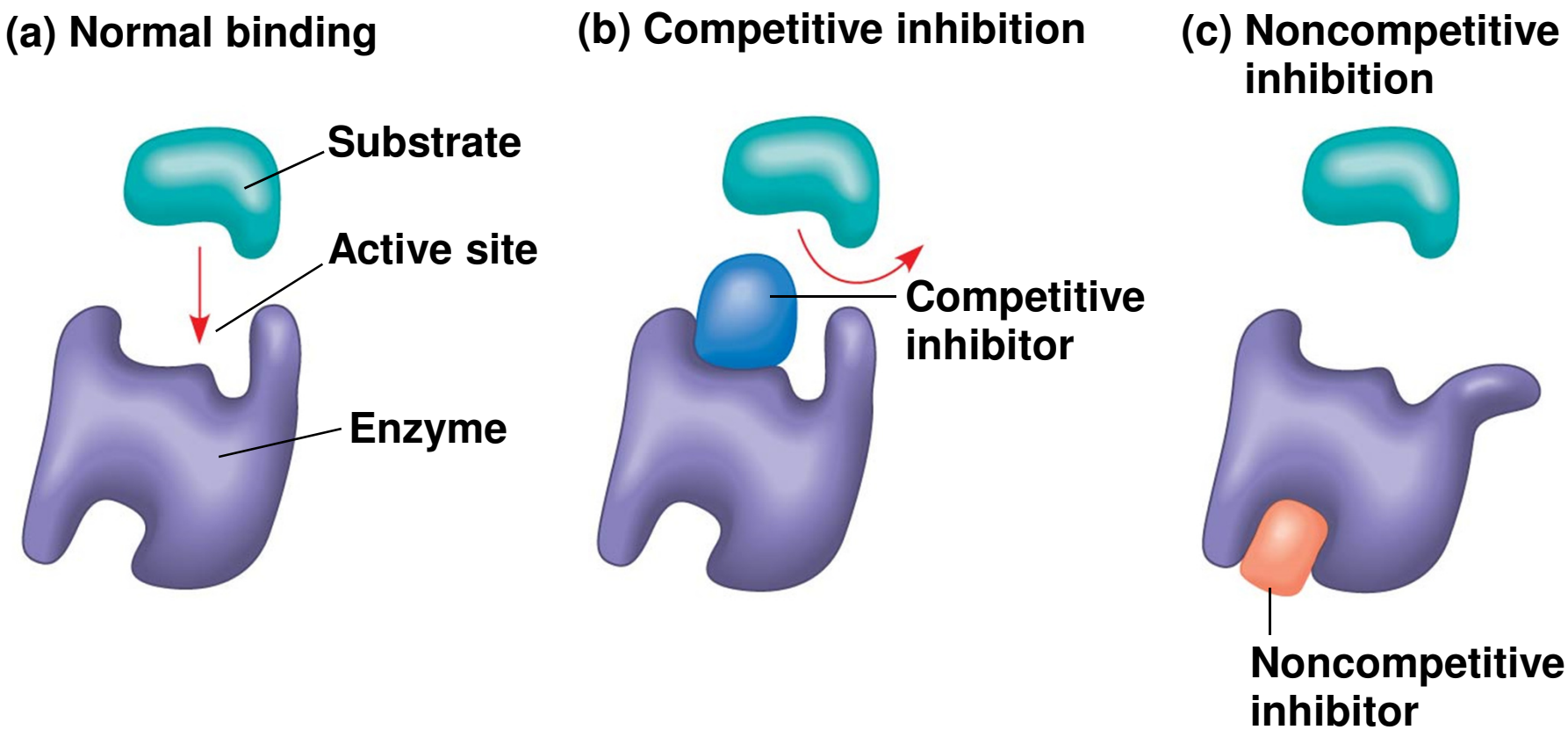
- If an inhibitor attaches to the enzyme by covalent bonds, inhibition is usually irreversible
- If an inhibitor binds by weak interactions, it can be reversible

- Examples of inhibitors include toxins, poisons, pesticides, and antibiotics
- Selective inhibition is essential to the control of cellular metabolism

Enzyme Inhibitors

- **Competitive inhibitors** mimic the normal substrate and bind to the active site of an enzyme
  - Block substrates from entering active sites, competing with the substrate
  - Can be overcome by increasing concentration of substrate
- **Noncompetitive inhibitors** bind to another part of an enzyme, causing the enzyme to change <u>shape</u> and making the active site less effective
  - Do not directly complete with substrate

Figure 6.17


(a) Normal binding
Substrate
Active site
Enzyme
(b) Competitive inhibition
Competitive inhibitor
(c) Noncompetitive inhibition
Noncompetitive inhibitor

The Evolution of Enzymes

- Enzymes are proteins encoded by genes
- Changes (mutations) in genes lead to changes in amino acid composition of an enzyme
- Altered amino acids in enzymes may alter their substrate specificity
- Under new environmental conditions a novel form of an enzyme might be favored

Concept 6.5: Regulation of enzyme activity helps control metabolism

- Chemical chaos would result if a cell's metabolic pathways were not tightly regulated
- A cell does this by switching on or off the genes that encode specific enzymes or by regulating the activity of enzymes

Allosteric Regulation of Enzymes

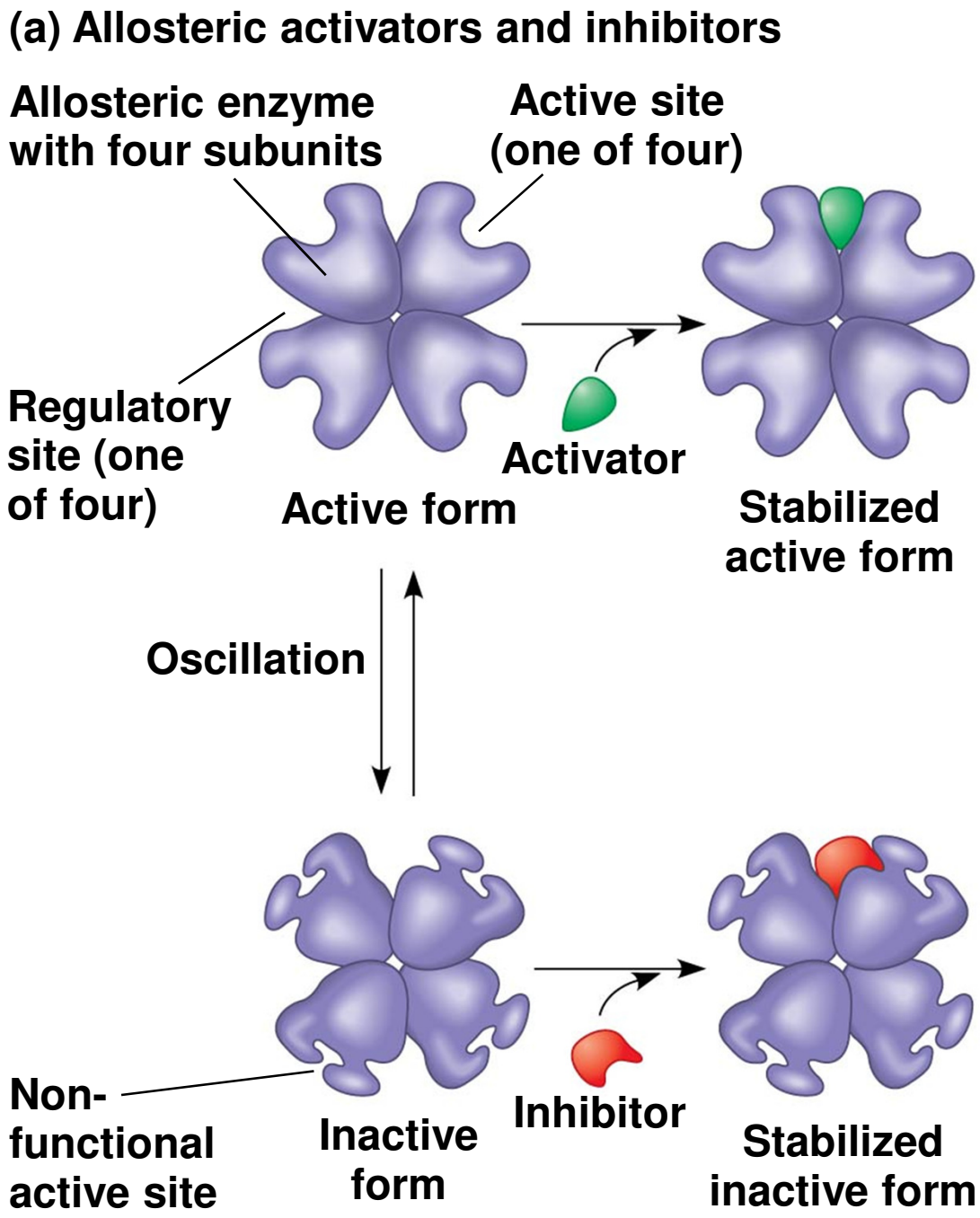
- Regulatory molecules change an enzyme's shape and the functioning of its active site
  - Bind elsewhere, via noncovalent interactions
  - Similar to reversible noncompetitive inhibitors
- **Allosteric regulation** occurs when a regulatory molecule binds to a protein at one site and affects the protein's function at another site
  - May either inhibit or stimulate an enzyme's activity

Allosteric Activation and Inhibition

- Each enzyme has active and inactive forms
  - The binding of an activator stabilizes the active form of the enzyme
  - The binding of an inhibitor stabilizes the inactive form of the enzyme

- ATP acts as in inhibitor of several catabolic enzymes
- ADP functions as an activator
  - Activates enzymes that speed up catabolism, producing more ATP

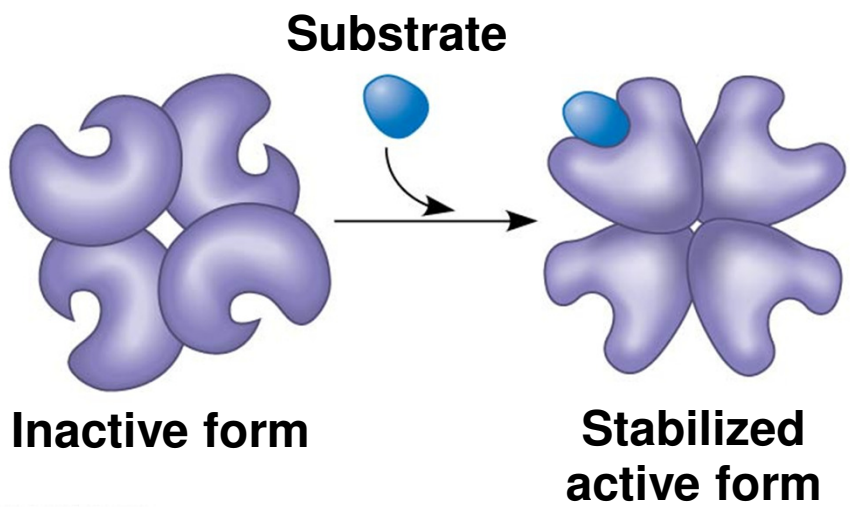
Figure 6.18a


(a) Allosteric activators and inhibitors
Allosteric enzyme with four subunits
Active site (one of four)
Regulatory site (one of four)
Activator
Active form
Stabilized active form
Oscillation
Non-functional active site
Inactive form
Inhibitor
Stabilized inactive form

- **Cooperativity** is a form of allosteric regulation whereby a substrate binds to one active site, triggering a shape change that facilitates binding of additional substrates
  - Can amplify enzyme activity
  - One substrate molecule primes an enzyme to act on additional substrate molecules more readily
- Cooperativity is allosteric because binding by a substrate to one active site affects catalysis in a different active site

Figure 6.18b

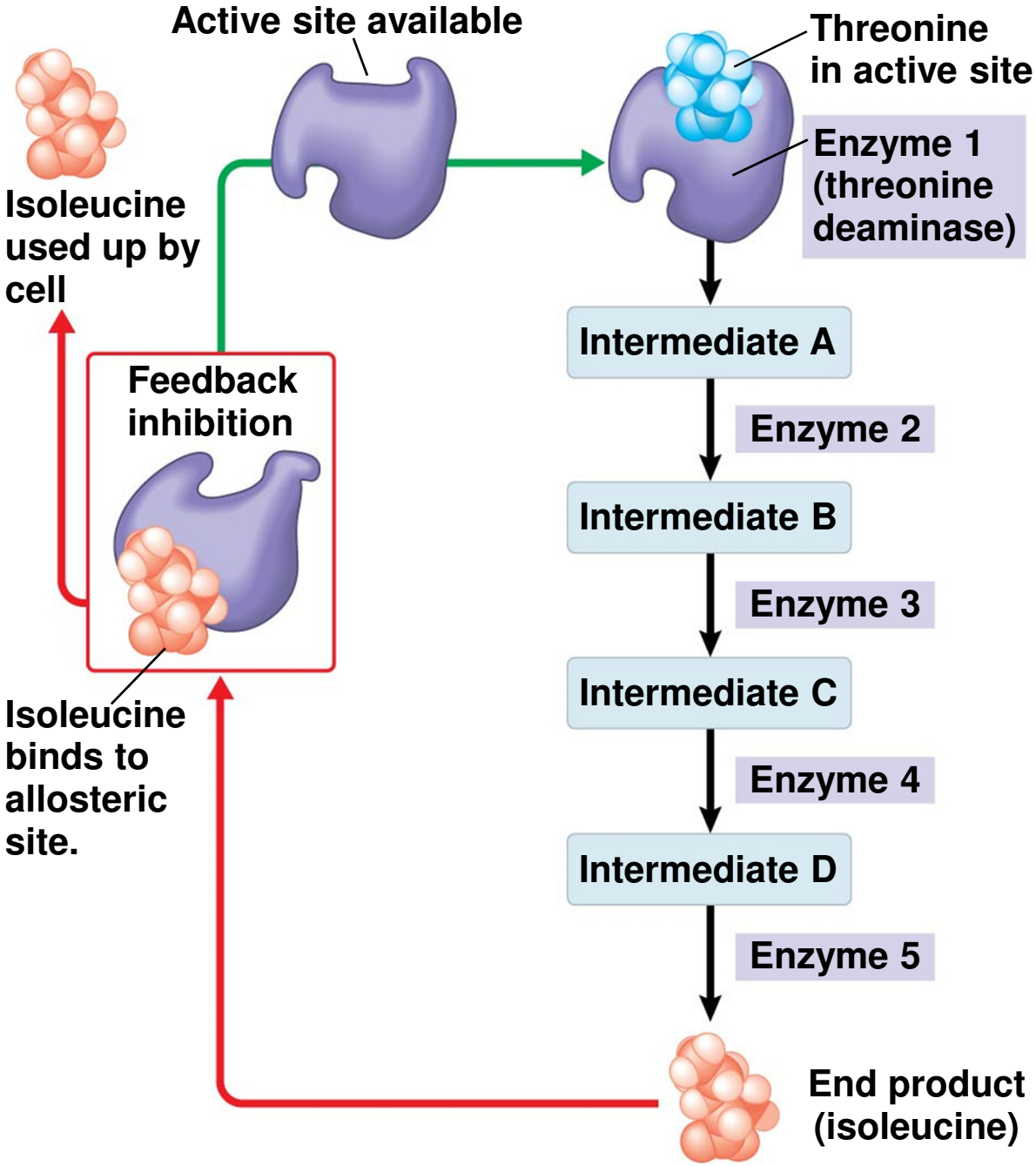
(b) Cooperativity: another type of allosteric activation



Feedback Inhibition

- In **feedback inhibition**, the end product of a metabolic pathway shuts down the pathway
- Feedback inhibition prevents a cell from wasting chemical resources by synthesizing more product than is needed

Figure 6.19


Active site available
Threonine in active site
Enzyme 1 (threonine deaminase)
Isoleucine used up by cell
Feedback inhibition
Intermediate A
Enzyme 2
Intermediate B
Enzyme 3
Intermediate C
Enzyme 4
Intermediate D
Enzyme 5
Isoleucine binds to allosteric site.
End product (isoleucine)

Specific Localization of Enzymes Within the Cell

- Structures within the cell help bring order to metabolic pathways
- Some enzymes act as structural components of membranes
- In eukaryotic cells, some enzymes reside in specific organelles
  - Ex: Enzymes for cellular respiration are located in mitochondria